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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/972,031	10/04/2001	Eugeni Namsaraev	STAN-202	2881

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EXAMINER	
JOHANNSEN, DIANA B	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/972,031	NAMSARAEV ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/31/03, 12/8/03, and 2/17/04*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *34-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

1. This action is responsive to the Amendment filed October 31, 2003, and to the Supplemental Amendment filed February 17, 2004 (which was a legible copy of a Supplemental Amendment originally filed December 8, 2003). Claims 1, 5-8, 10-14, 23, 25-30, 32-33, and 45 have been amended, and claims 1-33 and 45 are now under consideration. Applicants' arguments have been thoroughly considered, but are not persuasive for the reasons that follow. **This action is FINAL.**

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restriction

3. Applicant's election without traverse of Group 1, claims 1-33 and 45, in the Response filed April 14, 2003, is again acknowledged. Claims 34-44 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 112

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS' AMENDMENTS TO THE CLAIMS:

4. Claims 1-33 and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-33 and 45 are indefinite over the recitation of the terms "specific duplex(es)" in claim 1 and "specific nucleic acid duplex" in claim 45. The specification

does not provide a definition for this terminology, and it is not clear how a "specific" duplex having "a perfectly matched region of complementary" would differ from any other type of duplex having this property. While it is noted that the specification does define the term "specific association," this language merely requires that two molecules associate with "high specificity." This language is not clear and limiting, and further, there is no indication in the specification that, e.g., a "specific" duplex is once that requires or includes a "specific association." Accordingly, it is not clear how or whether the term "specific" further limits the duplexes of the claims.

Claims 1-33 are indefinite over the recitation of the phrase "whereby differences in the extent of specific duplex formation discriminate between matched and mismatched duplex regions at the level of a single nucleotide difference" in claim 1. First, it is unclear whether this recitation refers to differences within a single duplex, or to differences, e.g., in one duplex as compared to other duplexes. Further, it is again noted that the manner in which the term "specific" modifies the claims is unclear, such that it is not apparent how "specific duplex formation" would differ from "duplex formation." Clarification is required.

Claim 29 is indefinite over the recitation of the limitation "wherein said hybridization reaction comprises less than about 0.7M total ionic salt concentration." As the claim recites the open transitional language "comprises," it is unclear as to how or whether the further recitation "less than about 0.7M total ionic salt concentration" limits the claim. Clarification is required.

Claims 32-33 are indefinite over the recitation of the limitation "adding salt to said hybridization reaction until said hybridization reaction comprises greater than 0.7M total ionic salt concentration" in claim 32. It is noted that claim 1 (from which claim 32 depends) does not require any particular salt concentration. Accordingly, to the extent that claim 1 is drawn to methods in which the total ionic salt concentration is greater than 0.7M, it is unclear how claim 32 would further limit claim 1. For example, would claim 32 require the addition of salt in such a case? Clarification is required.

Claim Rejections - 35 USC § 102

5. Claims 1-33 and 45 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Cronin et al (U.S. 6,027,880 [2/2000; filed 10/1995]), for the reasons set forth in the Office action of July 30, 2003.

The Response of October 31, 2003 traverses the rejection on the following grounds. The Response argues that while reagents such as CTAB were previously known to accelerate association of nucleic acids, Applicants have determined that such reagents also increase the "specificity or selectivity of formation of completely matched duplexes over mismatched ones" under certain conditions. The Response urges that "a disclosure of an agent that improves specificity of hybridization is not a disclosure of an agent that both improves specificity and accelerates the hybridization reaction – that is, a disclosure of a specific association enhancer – as required by applicants' claims." Additionally, the response argues that the Cronin patent "does not in fact exemplify the use of CTAB as a specificity enhancing reagent," and further states that "Nor is CTAB mentioned, described, or taught elsewhere in the Cronin patent to be an agent capable

of enhancing specificity of hybridization." The response argues that the "elevated salt concentration used by Cronin in hybridizations containing CTAB" would preclude CTAB functioning as a "specificity enhancing agent" (referring to column 47, lines 45-60 of Cronin), and notes a teaching in the specification that increased ionic salt concentrations disrupt "the association of the specific association enhancer and nucleic acid duplex." Finally, the response argues that "Cronin neither mentions, describes, nor teaches that either betaine or TMAC....can serve as hybridization accelerants."

These arguments have been thoroughly considered but are not persuasive. First, it is again noted that Cronin et al exemplify the use of CTAB, and that CTAB is specifically recited in Applicants' claims (and disclosed in the specification) as a preferred "specific association enhancer." The fact that Cronin et al do not teach or disclose the same properties of CTAB that are disclosed in Applicants' specification does not obviate the fact that Cronin et al exemplify the use of CTAB, and anticipate the claims. Properties possessed by CTAB are inherent to it, and need not be explicitly stated in order for the Cronin et al reference to be anticipatory. With regard to Applicants' argument that the conditions (and particularly the salt concentration) exemplified by Cronin et al would prevent CTAB from functioning as a specific association enhancer, it is noted that neither the limitations in the claims, nor the teachings of the specification, indicate that the conditions employed by Cronin et al would not be encompassed by the claims, or would preclude the functioning of CTAB in such a manner. It is agreed that Cronin et al teach dilution of PCR products "10 to 25 fold into 5X SSPE (750 mM NaCl, 50 mM NaPhosphate, 5 mM EDTA, pH 7.4)...and 1

mM" CTAB. However, the instant claims clearly encompass such conditions: even the most restrictive claim with respect to salt concentration (claim 29) merely requires that "said hybridization reaction comprises less than about 0.7M total ionic salt concentration," and the specification at, e.g., page 19, merely indicates that "preferably" total ionic salt concentrations "should not exceed about 0.7 M." Accordingly, none of the pending claims are limited in such a way that would exclude the conditions of Cronin et al (in particular, it is noted that Cronin et al teach dilution of PCR products in 5X SSPE, which dilution would result in a reduced overall salt concentration, and further that the language "about 0.7M" is imprecise and would not, even in the absence of the "comprises" language in claim 29, limit the claims to exactly 0.7M). Finally, regarding Applicants' argument that "Cronin neither mentions, describes, nor teaches that either betaine or TMAC...can serve as hybridization accelerants," this argument is not persuasive: no such teaching is required in order for the Cronin et al reference to anticipate the claims, which it does, for the reasons discussed above and in the prior Office action. With further regard to claim 32, it is noted that Cronin et al disclose steps of washing with a solution of 5X SSPE (undiluted) following hybridization (see column 47, lines 58-60), and thereby disclose adding salt and increasing the "total ionic salt concentration" (as well as "removing or diluting said specific association enhancer," as was stated in the prior Office action).

In the Response filed February 17, 2004, with regard to the examiner's summary of the Interview conducted November 20, 2003, Applicants further argue that while "CTAB may have been a known compound, the prior art does not disclose a method of

use of CTAB that would provide for CTAB to behave as a specific association enhancer." Applicants continue that "the claimed invention is not simply directed to use of CTAB in a hybridization reaction," but that the claimed invention is "generally directed to performing hybridization reactions under conditions suitable for accelerated association of the first and second molecules in a specific nucleic acid duplex so as to allow for discrimination between matched and mismatched duplexes at the level of a single nucleotide difference." These arguments are not persuasive for the same reasons given above. Specifically, as the conditions disclosed by Cronin et al meet the requirements of the claims, the reference is anticipatory, irrespective of whether the reference does or does not teach the same advantages of the invention disclosed by Applicants.

The Cronin et al reference discloses all the limitations of present claims 1-33 and 45, and therefore this rejection is maintained.

6. Claims 1-33 and 45 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Cronin et al (U.S. 6,027,880 [2/2000; filed 10/1995]), for the reasons set forth in the Office action of July 30, 2003.

The Response traverses the rejection for the same reasons discussed in paragraph 5, above. Accordingly, the response to those arguments applies equally herein.

The Cronin et al reference discloses all the limitations of present claims 1-33 and 45, and therefore this rejection is maintained.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 571/272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Diana B. Johannsen
Primary Examiner
June 17, 2004